IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Patent Application No. 10/526,851

Applicant: Kozikowski et al.

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Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

DECLARATION UNDER 37 C.F.R. § 1.132 FROM PHILLIP A. DENNIS

I, Phillip A. Dennis, hereby declare that:

1. I received a B.A. degree in 1984 from the University of Virginia in Charlottesville, VA, and M.S., Ph.D., and M.D. degrees in 1988, 1991, and 1992, respectively, from New York University School of Medicine, New York, NY. I have held a number of research, teaching, and physician positions since 1982 and am presently Senior Investigator, Medical Oncology Branch, Center for Cancer Research, National Cancer Institute, NIH, in Bethesda, MD.

2. I am a named co-inventor in the above-identified application, and am familiar with the application and the pending claims. Based on the tests carried out under my direction or supervision, compounds of the invention, SH-23 and SH-16, inhibit growth of cancer.

3. Compound designated as SH-23 in the patent application was tested for in vivo activity in polyvinylidene fluoride (PVDF) hollow fibers laden with cancer cells. Cells were grown inside PVDF fibers and inserted intraperitoneally (i.p.) or subcutaneously (s.c.) into compartments of nude mice. SH-23 was dissolved in 10% DMSO in saline and given

intraperitoneally every day for 4 days, with dosing beginning on the third day after fiber implantation at doses of 25 and 37.5 mg/kg. The results are set forth in Table 1 below.

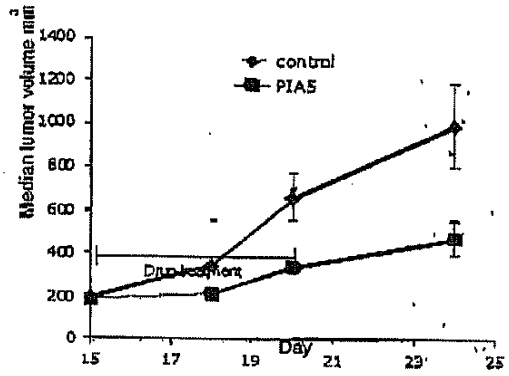
Table 1. In vivo efficacy of SH-23 in hollow fiber assays

Cancer cell type	i.p.	s.c.
H522	-	2
UACC-62	-	-
U251	-	-
H23	2	4
MDA-MB-231	-	-
SW620	2	2
MDA-MB-435	4	4
OVCAR-5	-	2
SF-295	4	2
LOX	2	-
COLO205	-	-
OVCAR-3	2	-
Total	16	16

A score of 2 indicates that growth was inhibited ≥50% within the fiber for a particular dose. The number 4 indicates it decreased growth ≥50% in hollow fibers in mice that received both the 25 and 37.5% mg/kg dose levels.

4. 5×10^6 human H157 non-small cell lung cancer cells were inoculated subcutaneously into athymic nude mice in both rear flanks. When tumors reached 200 mg, mice were randomized into vehicle or treatment groups, 15 mice/group, and treatment was initiated. 90 mg/kg compound SH-16 (or PIA5 in Figure 1) dissolved in 10% DMSO, 5% Tween 80 in saline or vehicle was injected i.p. daily for 5 days (days 15-20), and tumor volumes were followed for an additional 4 days. Tumor volumes were calculated from the formula $v = (ab^2)/2$, where a = long axis, b = short axis; $p<0.005$. The results obtained are shown in Figure 1.

Figure 1. Efficacy of PIA5 in H157 xenograft model.



5. I hereby declare that all statements made herein of my own knowledge are true, that all statements made on information and belief are believed to be true, that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code, and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: 5/14/07

Phillip A. Dennis, M.D., Ph.D.